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(21) International Application Number: PCT/US00/09512 (22) International Filing Date: 7 April 2000 (07.04.00) (30) Priority Data: 60/128,593 9 April 1999 (09.04.99) US (71) Applicant (for all designated States except US): SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH [US/US]; 1275 York Avenue, New York, NY 10021 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): ROSEN, Neal [US/US]; Office of Industrial Affairs, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10021 (US). KUDUK, Scott, D. [US/US]; Office of Industrial Affairs, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10021 (US). DANISHEFSKY, Samuel, J. [US/US]; Office of Industrial Affairs, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10021 (US). ZHENG, Furzhong, F. [CN/US]; Office of Industrial Affairs, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10021 (US). SEPP-LORENZINO, Laura [US/US]; Office of Industrial Affairs, Memorial Sloan Kettering Cancer Center, 1275		York Avenue, New York, NY 10021 (US). OUERFELLI, Ouathék [TN/US]; Office of Industrial Affairs, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10021 (US). (74) Agents: PARSONS, Nancy, J. et al.; Oppedahl & Larson LLP, P.O. Box 5068, Dillon, CO 80435-5068 (US). (81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>	
(54) Title: METHODS AND COMPOSITIONS FOR DEGRADATION AND/OR INHIBITION OF HER-FAMILY TYROSINE KINASES			
(57) Abstract Bifunctional molecules comprising two hsp-binding moieties which bind to hsp90 in the pocket to which ansamycin antibiotics bind connected via a linker are effective for inducing the degradation and/or inhibition of HER-family tyrosine kinases. For example, a compound of two geldanamycin moieties joined by a four-carbon linker provides selective degradation of HER-family tyrosine kinases, without substantially affecting other kinases. These compounds can be used for treatment of HER-positive cancers with reduced toxicity, since these compounds potentially kill cancer cells but affect fewer proteins than geldanamycin.			